REMARKS/ARGUMENTS

In this Amendment, the status of the claims is as follows: claims 1-49, 53, 76, 96, 105 and 106 have been canceled; claims 50-52, 54, 73-75, 77, 97, 98, 103 and 104 are currently amended; claims 55-72, 78-93, 99-102 and 107-131 were previously presented; and claims 94 and 95 are original claims. It is submitted that no new matter has been added by virtue of the amended claims, which are supported by the disclosure and claims of the application as originally filed and by the previously presented claims.

Specifically, support for at least two matrix-forming bulking/releasing agents as recited in the currently amended claims is found on page 6, last two lines to page 7, lines 1-5; on page 8, last three lines to page 9, lines 1-7; and in the Examples, Table 1, Formulation numbers 6, 7 and 9 on page 11 of the as-filed specification.

Accordingly, claims 50-52, 54-75, 77-95, 97-104 and 107-131 are currently pending in this application.

Applicants' Reiterated Request for Change of Correspondence/Mailing Address and Customer Number

Applicants again request that the correspondence/mailing address and customer number for this application be recognized as "MINTZ, LEVIN, COHN, FERRIS, GLOVSKY and POPEO, P.C., The Chrysler Center, 666 Third Avenue, New York, New York 10017, **Customer No. 35437** and officially changed in the U.S. Patent and Trademark Office.

As previously mentioned, Applicants submitted Form PTO/SB/122 "Change of Correspondence Address" in this application on October 8, 2004. A review of the Image File Wrapper for this application on the U.S. PTO PAIR website shows that the above Change of Correspondence Address paper and was received was date-stamped "OCT 08 2004" by the U.S. PTO.

On December 16, 2004, Applicants submitted a formal Revocation of Power of Attorney by Assignee, New Power of Attorney and Change of Correspondence Address document, along

with accompanying documentation, in this application. A review of the Image File Wrapper for this application on the U.S. PTO PAIR website shows that the Revocation of Power of Attorney by Assignee, New Power of Attorney and Change of Correspondence Address document was received and date-stamped "DEC 16 2004" by the U.S. PTO.

Although the Image File Wrapper for this application on the U.S. PTO PAIR website shows that the above papers were received by the U.S. PTO as-filed, there is a paper described as "Change of Address" and dated December 23, 2004, which is listed in the U.S. PTO PAIR Image File Wrapper. It appears from this paper that the U.S. PTO erroneously set both the correspondence address and the maintenance fee address to the prior customer number in this application rather than changing the correspondence address to the current address and customer number as Applicants have formally requested.

Accordingly, in view of the above information, appropriate correction of the Patent Office records to reflect the current correspondence address (i.e., MINTZ, LEVIN, COHN, FERRIS, GLOVSKY and POPEO, P.C., The Chrysler Center, 666 Third Avenue, New York, New York 10017) and customer number (i.e., Customer Number 35437) for this application is again requested.

Information Disclosure Statement

Applicants respectfully request that the Examiner return an initialed copy of the Form PTO 1449 as submitted with the Supplemental Information Disclosure Statement on August 1, 2005 in this application.

The claims fulfill the requirements of 35 U.S.C. § 103(a)

WO 98/07414

Claims 50-52, 54-75, 77-95, 97-104 and 107-131 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over previously-cited international publication, WO 98/07414.

The Examiner alleges that WO 98/07414 "discloses the same process of preparation for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are

coated with at least two surfactants; one of the surfactants is a phospholipid (surface acting agent)". The Examiner cites to the paragraph bridging pages 7 and 8 of WO 98/07414 as teaching that mannitol and other agents may be added to adjust the final formulation to isotonicity as well as a stabilizing agent during drying. According to the Examiner, from this teaching it would have been obvious to one of ordinary skill in the art that "the addition of mannitol is a manipulatable parameter", which can be added "either before or after the homogenization step with the expectation of obtaining the best possible stabilized product." The Examiner has opined that Applicants' previous arguments are not persuasive because the amount of mannitol in the examples of WO 98/07414 appear to fall into the range of bulking agent claimed by Applicants, and one would expect that mannitol would have the same properties in the instant invention as disclosed in WO 98/07414. (10/19/05 Office Action, page 4).

Applicants respectfully disagree with and traverse this rejection.

It is well understood that a claimed invention must be considered as a whole in determining differences between the prior art and the claimed invention. M.P.E.P. §2141.02. In addition, all claim limitations must be taught or suggested by the cited art reference. M.P.E.P. §2143.03. In the instant case, the presently claimed process, considered in its entirety, involves inventive steps and associated components and functional results which WO 98/07414 fails to teach, disclose, or suggest.

First, it is pointed out that the invention contemplated and disclosed by WO 98/07414 is a process of making non-aggregating, submicron sized primary microparticles and the particles so produced. The cited reference also does not disclose or describe a rapidly dispersible solid dosage form of a drug, for example, in tablet form, or a process to prepare such a rapidly dispersible drug dosage form. It is submitted that the presently claimed invention draws on and furthers the teaching in the art by describing a new process of preparing a rapidly disintegrating solid dosage form comprising microparticles of a water insoluble or poorly water soluble drug.

More specifically, WO 98/07414 is silent regarding a process of preparing a rapidly disintegrating solid dosage form containing fenofibrate microparticles. Nowhere in WO

98/07414 is there a teaching that at least two, rapidly dispersible, matrix-forming bulking/releasing agents are admixed with, or included during the process of preparing, the microparticles disclosed by WO 98/07414. Nowhere in WO 98/07414 is there a teaching of a process that includes the formation of a solid support matrix wherein drug-containing particles are dispersed and embedded throughout, and also wherein this support matrix dissolves or disperses in a rapid disintegration time when the solid matrix contacts an aqueous environment. Nor does WO 98/07414 contain teaching that at least two, rapidly dispersible, matrix-forming bulking/releasing agents are present in a specified amount in a process of making a rapidly dispersing solid dosage form of a drug having the functions specified according to the presently claimed invention. The foregoing teachings are newly provided to the art by Applicants and are not found in WO 98/07414.

In addition to the distinct lack of teaching and disclosure in the cited WO 98/07414 reference, it is submitted that the skilled practitioner in the pertinent art, who is trying to prepare or formulate a stabilized, solid dosage form, e.g., a tablet form, of a drug, wherein the dosage form is also rapidly dispersible, is beset by and must overcome various problems and difficulties. Applicants' presently claimed invention addresses and provides a solution to these problems and difficulties.

In particular, although useful as ingredients in pharmaceutical preparations to stabilize primary particles of drug substances, phospholipids, e.g., lecithin, are by their very nature both extremely hygroscopic and water insoluble. These characteristics can adversely affect the integrity of a solid dosage form, e.g., a tablet form, of a drug, particularly under conditions of high humidity. See, for example, the mention of such characteristics in the attached document entitled "Lecithin", as taken from the *Handbook of Pharmaceutical Excipients*, Third Edition, Ed., A. Kibbe, American Pharmaceutical Association and the Pharmaceutical Press, 2000, pp. 292-294.

Faced with the hygroscopic nature and insolubility problems of phospholipids such as lecithin, the ordinarily skilled artisan who is in the business of preparing a stable solid dosage form of a water insoluble drug which is ultimately rapidly dispersible upon use, would not be motivated or compelled to use phospholipid as a surface stabilizing ingredient of the dosage

form, such as a drug tablet. This is because the mechanical strength and/or dispersibility properties of the resulting solid dosage drug form or tablet could be adversely affected by the hygroscopic and insolubility properties of the phospholipids. For example, the notion of using hygroscopic phospholipid as a surface stabilizer in a solid dosage drug form would be readily dismissed by the ordinarily skilled artisan, since solid drug dosage forms, e.g., drug tablets, are often stored in highly humid conditions, such as in users' bathroom medicine cabinets. Thus, the skilled person in the art would have little or no incentive to utilize phospholipid stabilizers in the preparation of a solid dosage drug form, or to employ the teaching of WO 98/07414 to the preparation of a solid dosage drug form, since WO 98/07414 advocates preparing primary microparticles with phospholipid in conjunction with other surface acting agents.

While WO 98/07414 discloses the preparation of primary microparticles stabilized with surface acting agents including phospholipid, this reference does not disclose or teach the preparation of a solid dosage form of a drug, such as a tablet, that is mechanically robust throughout its shelf life and its in-use life. In essence, WO 98/07414 discloses only a first portion, or a first stage, i.e., making stabilized primary particles, involved in the preparation of a solid dosage form containing a water insoluble drug. In contrast, Applicants' presently claimed invention provides a complete process of making a solid dosage drug form that is stable and rapidly dispersible upon aqueous contact. Applicants' invention must be considered as a whole, and as such, provides an inventive process that advances the art from the preparation of primary particles, as described in WO 98/07414, to the complete preparation of a solid dosage drug form that is both stable over time and rapidly dispersible in an aqueous environment upon use.

Moreover, confronted with the disclosure and teaching of WO 98/07414 and appreciating the hygroscopic and insoluble nature of phospholipids as known in the art, one skilled in the art who is preparing more than primary microparticles, that is, one who is preparing a solid dosage form of a drug that is both stable and highly dispersible, would not be led by WO 98/07414 to utilize phospholipids in preparing the solid drug dosage form, particularly particles, granules, or powders that are to be formed into solid tablets. Even though phospholipids, along with other agents, may be suitable for stabilizing primary particles, phospholipids are understood by those having skill in the art to be particularly unsuitable, or

even considered to be antithetical, for formulating into a solid drug dosage form because they are hygroscopic, have unfavorable bulk properties and are difficult to handle. Thus, the present claims drawn to a rapidly dispersible solid drug dosage form and a process of preparing the same are inventive and nonobvious in view of the cited references, in combination.

In addition, Applicants submit that to characterize WO 98/07414 as disclosing "the same process" as the instant invention for the preparation of rapidly dispersing oral dosage forms, as opined by the Examiner at page 2 of the 10/19/2005 Office Action, is without basis in the cited art reference. WO 98/07414 does not remotely teach the totality of the steps and elements required by Applicants' presently claimed process of producing rapidly disintegrating solid dosage forms of drugs.

WO 98/07414 teaches stabilized primary microparticles that do not aggregate, and a process for their preparation. WO 98/07414 does not teach Applicants' process in which microparticles, such as, for example, those taught by WO 98/07414, are further utilized as components in a process that results in drug microparticles being dispersed and embedded throughout a solid support matrix comprising at least two bulking/releasing agents, thus yielding the solid drug dosage forms that are rapidly dissolved and/or disintegrated to rapidly release drug microparticles upon contact with an aqueous environment. WO 98/07414 also fails to teach or suggest that a suspension of drug-containing microparticles resulting from contact of a microparticle-embedded, solid support matrix and an aqueous environment comprises no more than about 20% by weight of aggregated or agglomerated primary particles, as described for the presently claimed invention.

WO 98/07414 discloses that its contemplated primary microparticles may be prepared using surface modifying agents and that mannitol may be added to adjust the final formulation to isotonicity as well as a stabilizing aid during drying. (page 8, lines 4-6 of WO 98/07414). The Examples of WO 98/07414 show mannitol as an ingredient in the disclosed formulations to make primary microparticles or suspensions thereof. The Examiner has cited to this teaching of WO 98/07414 and has expanded it, without basis in the disclosure of WO 98/07414, to encompass other steps and components of the presently claimed process that are simply not taught or suggested by WO 98/07414.

The Examiner opines that it would have been obvious to one of ordinary skill in the art from the teaching of WO 98/07414 that the addition of mannitol is a manipulatable parameter (i.e., it can be added either before or after the homogenization step) with the expectation of obtaining the best possible stabilized product. (10/19/2005 Office Action, page 3). However, the presently claimed invention is drawn to a process of making a rapidly dispersible solid dosage drug form and, as such, is directed to more than just a stabilized preparation of primary microparticles.

Indeed, the distinctions between the invention contemplated by WO 98/07414 and the presently claimed process and the results thereof are clear from the teachings of the instant specification. For example, at page 6, last two lines to page 7, lines 1-5, the as-filed specification describes a process that is reflected in the present claims, as follows:

> The resulting homogeneous suspension of microparticles stabilized by one or more surface modifiers is then mixed with matrix-forming bulking and/or releasing agents (dry or as an aqueous solution) and is then dried. The bulking or matrix-forming agent provides a mass in which the particles of drug are embedded or retained. The release agent assists in disintegration of the matrix when it contacts aqueous media. The bulking/releasing agents are chosen in order to produce a support matrix that, upon drying, will yield rapidly dispersible tablets that release the primary particles upon reconstitution in aqueous medium.

The specification further teaches at page 8, last three lines to page 9, lines 1-7, that

> The matrix-forming agent used in the present invention must dissolve or disperse upon contact with an aqueous environment and release the phospholipid coated therapeutic agent particle. Upon reconstitution, the product reverts to a suspension having the same degree of dispersity as the pre-dried suspension, with preferably no more than 20% by weight ... of aggregated primary particles as revealed by particle sizing and microscopic methods known in the art. Surprisingly, the freeze-dried suspension prepared according to the present invention can be stored for extended periods of time, even at high temperature and humidity, without loss of this redispersibility characteristic upon reconstitution and thus is essentially devoid of particle aggregation.

Additionally, Applicants' rapidly dispersible solid dosage forms containing at least two matrix-forming bulking/releasing agents, or combinations thereof, prepared according to the presently claimed invention, are exemplified in the instant specification, for example, in Table 1, Formulations 6, 7 and 9, at page 11. By contrast, WO 98/07414 teaches and exemplifies only surface modified primary microparticles containing a water insoluble or poorly water soluble substance, and the preparation thereof, wherein mannitol may be an ingredient.

It is submitted that Applicants' above-mentioned disclosure, which supports and is unique to the instant invention, is not "an obvious disclosure of the prior art's teaching", as alleged by the Examiner on page 3 of the 10/19/2005 Office Action. Applicants' presently claimed process of preparing a readily dispersible solid dosage form of drug-containing microparticles, which includes new and unobvious steps of admixing primary microparticles with at least two matrix-forming bulking/releasing agents, or admixing at least two matrix-forming bulking/releasing agents with components to produce a rapidly dispersing solid support matrix in which the drug microparticles are embedded yet releasable, is not within the scope of the teaching of WO 98/07414.

Based on the clear teaching and disclosure of WO 98/07414, one skilled in the art is taught and would expect a process that produces non-aggregating primary microparticles, and not a process that includes particular steps and elements to produce a drug dosage form characterized by a solid support matrix in which drug-containing component microparticles are dispersed and embedded as a result of the process, wherein the so-formed solid matrix disperses rapidly to release a suspension of non-aggregating drug microparticles upon contact with an aqueous environment, as required by Applicants' invention. The steps, components and functional results that comprise the process of making a rapidly disintegrating solid drug dosage form according to the presently claimed invention are patentably distinct from the primary microparticles and the process of making them as disclosed in WO 98/07414.

Furthermore, the claimed invention as a whole must be considered in making a determination of obviousness. *See,* M.P.E.P. § 2141.02 (I) and citations therein. In view of this requirement, it is submitted that Applicants' presently claimed invention, considered as a whole, contains multiple steps that are distinguished from and are unobvious over WO 98/07414.

In particular, WO 98/07414 teaches fewer, i.e., essentially two, steps in a method that results only in the formation of primary microparticles of a certain dimension. That other steps might be added to the process of WO 98/07414 does not negate the patentability of the present invention in view of WO 98/07414, as the cited document does not disclose or exemplify any teaching that would lead one skilled in the art to arrive at all of Applicants' process steps, considered as a whole, or to achieve the functional results of a rapidly dispersible solid dosage drug form that are required according to Applicants' invention.

Similarly, it is impermissible to distill Applicants' presently claimed invention down to a "gist" or "thrust", as this disregards the requirement of analyzing the subject matter as a whole. *See,* M.P.E.P. § 2141.02 (II) and citations therein. Distilling the presently claimed invention down to two steps, which may or may not include mannitol and which merely result in the formation of stabilized primary microparticles, restricts consideration of and disregards the other limitations that comprise the entirety of the steps of Applicants' presently claimed invention. All of the claim limitations must be taught or suggested by the prior art. *See,* M.P.E.P. § 2143.03 and citations therein.

Based on the complete disclosure and teachings of WO 98/07414, which is limited to stabilized and non-aggregating primary microparticles and a process for their preparation, it is submitted that it would not have been obvious for one having skill in the art to arrive at and employ all of the particular and additional steps, elements and functions thereof, as recited in Applicants' claims, to produce a rapidly disintegrating solid dosage form of water insoluble or poorly water soluble drug-containing microparticles. The presently claimed invention and the teachings and contemplated invention of WO 98/07414 are patentably distinct from and unobvious in view of each other.

It is also well settled that it is impermissible to invoke hindsight reconstruction to determine that the instantly claimed process is made obvious by WO 98/07414. Applicants' present claims are drawn to a distinctly different process comprising similar, but further and importantly, additional and distinguishing steps and components that function together in a nonobvious manner to achieve a nonobvious result.

It is respectfully submitted that it is also impermissible to attribute steps and functions recited in the instantly claimed process, considered as a whole, to the teaching of WO 98/07414 in the absence of a basis in WO 98/07414 that would motivate one to do so. Steps and functional limitations that are recited in the instant claims and found in the instant specification cannot be *a priori* ascribed to WO 98/07414 without proper support, teaching, or suggestion from the art reference. Accordingly, in view of the nonobvious differences between the presently claimed invention and the teaching and extent of the disclosure of WO 98/07414, it is respectfully requested that this rejection be withdrawn.

Neither the statement that mannitol "may be added to adjust the final formulation to isotonicity as well as a stabilizing aid during drying" nor the examples in WO 98/07414 provides motivation or impetus for the skilled practitioner to modify the method of WO 98/07414 by adding the various steps and components as taught and required by Applicants' invention to arrive at Applicants' presently claimed process of making a rapidly dispersible dosage form of a drug. Applicants' own disclosure provides the additional teaching that is needed to arrive at Applicants' claimed process.

In sum, the totality of the steps, elements and functional requirements in Applicants' presently claimed process, considered as a whole, are not made obvious by the disclosure of WO 98/07414. Based on the disclosure of WO 98/07414 for all that it teaches, WO 98/07414 neither discloses nor suggests all of Applicants' claim limitations, as is required for an obviousness determination pursuant to M.P.E.P. §2143. Consequently, WO 98/07414 fails to make obvious Applicants' invention as presently claimed. In view of the foregoing, it is submitted that a *prima facie* case of obviousness of the presently claimed invention has not been shown. Withdrawal of this rejection is thus respectfully requested.

Double Patenting

U.S. Patent No. 5,922,355

Claims 50-52, 54-75, 77-95, 97-104 and 107-131 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-11 of U.S. Patent No. 5,922,355 ("the '355 patent"). The Examiner states that the

conflicting claims are not identical, but are allegedly not patentably distinct from each other because the claims in the '355 patent, which are drawn to "a process of preparing microparticles of water insoluble drugs mixing the drug, a phospholipid and another surfactant and applying energy to reduce particle sizes", recite comprising language and that "applicant's intent to include bulking material such as mannitol in the comprising language is clear from the examples" in the cited patent. The Examiner opines that the "instant steps of adding the bulking materials" are deemed to be included in the patented method claims.

Applicants disagree with this rejection and submit that although the claims of the '355 patent contain comprising language, there is no teaching or disclosure in the '355 patent that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success.

The teaching of the '355 patent is limited to the production of microparticles of certain dimensions. Unlike the presently claimed invention, the '355 patent contains no teaching or disclosure of further steps other than those involved in making the microparticles. To assume that the comprising language of the claims of the '355 patent encompasses the particular steps recited in Applicants' presently claimed invention is also without basis, since the disclosure of the '355 patent does not teach the additional steps of admixing at least two matrix-forming bulking/releasing agents, or a combination of matrix-forming bulking agent and matrix-forming releasing agent to the microparticles described in the patent, and drying the admixture so as to produce a solid matrix having microparticles embedded and dispersed therein, wherein the solid matrix is rapidly dispersible in aqueous medium according to the additional steps of the presently claimed invention.

The combination of steps and elements of the presently claimed invention, including at least two matrix-forming bulking/releasing agents and combinations thereof, contributes to the newly described properties of high dispersibility imparted to the solid dosage drug form that is produced by Applicants' presently claimed process. The totality of the steps and elements that constitute the process of the presently claimed invention are not at all found in the disclosure of the '355 patent. The '355 patent claims processes of preparing or stabilizing microparticles, as well as compositions produced by the processes. The patent does not teach Applicants'

presently claimed process of preparing a rapidly dispersible solid dosage form containing drug microparticles.

In fact, the presently claimed process, while including the use of microparticles such as described in the '355 patent, may be considered to further and extend the teaching of the '355 patent in a novel and unobvious way. Unlike the '355 patent, the presently claimed invention as a whole involves newly designed steps in which additional components are admixed with microparticles, e.g., as recited in steps (c) - (f) of the presently claimed invention, to arrive at Applicants' rapidly dispersible solid dosage form having the new and unobvious properties achieved according to the present invention.

However, without the teachings of Applicants' own invention, there is no disclosure or suggestion provided in the '355 patent that allows one skilled in the art to know to include the additional steps of admixing at least two matrix forming bulking/releasing agents with drug-containing microparticles, or during the formation of such microparticles, and drying the admixture to produce a rapidly dispersible solid drug dosage form in which drug-containing microparticles are dispersed and embedded in a solid support matrix having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the invention of Applicants.

The '355 patent simply does not teach or contemplate Applicants' process of producing a rapidly dispersible solid matrix form of a drug. Specific and nonobvious steps and components of Applicants' claimed process that are not supported by the disclosure and teaching of the '355 patent cannot *a priori* be determined to be included in the patent's process despite the use of comprising language in the claims. Accordingly, the '355 patent does not make obvious the presently amended claims. Withdrawal of this rejection is respectfully requested.

U.S. Patent No. 6,228,399

Claims 50-52, 54-75, 77-95, 97-104 and 107-131 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-5 of U.S. Patent No. 6,228,399 ("the '399 patent"). The Examiner states that the conflicting claims are not identical, but are allegedly not patentably distinct from each other

because the claims in the '399 patent, which are drawn to "a process of preparing microparticles of water insoluble drug, cyclosporine by mixing the drug, a phospholipid and another surfactant and applying energy to reduce particle sizes", recite comprising language and that "applicant's intent to include bulking material such as mannitol in the comprising language is clear from the examples" in the cited patent. The Examiner opines that the "instant steps of adding the bulking materials" are deemed to be included in the patented method claims and that "water insoluble drug includes cyclosporine" in the '399 patent claims.

Applicants disagree with this rejection and submit that although the claims of the '399 patent contain comprising language, there is no teaching or disclosure in the '399 patent that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success.

The teaching of the '399 patent is limited to the production of cyclosporin microparticles of certain dimensions. Unlike the presently claimed invention, the '399 patent contains no teaching or disclosure of further steps other than those involved in making the microparticles. To assume that the comprising language of the claims of the '399 patent encompasses the particular steps recited in Applicants' presently claimed invention is also without basis, since the disclosure of the '399 patent does not teach the additional steps of admixing at least two matrix-forming bulking/releasing agents, or a combination of matrix-forming bulking agent and matrix-forming releasing agent, to the microparticles described in the patent, and drying the admixture so as to produce a solid matrix having microparticles embedded and dispersed therein, wherein the solid matrix is rapidly dispersible in aqueous medium according to the additional steps of the presently claimed invention.

The combination of steps and elements of the presently claimed invention, including at least two matrix-forming bulking/releasing agents and combinations thereof, contributes to the newly described properties of high dispersibility imparted to the solid dosage drug form that is produced by Applicants' presently claimed process. The totality of the steps and elements that constitute the process of the presently claimed invention are not at all found in the disclosure of the '399 patent. The '399 patent claims processes of preparing cyclosporin microparticles. The

patent does not teach Applicants' presently claimed process of preparing a rapidly dispersible solid dosage form containing drug microparticles.

In fact, the presently claimed process, while including the use of microparticles such as those described in the '399 patent, may be considered to further and extend the teaching of the '399 patent in a novel and unobvious way. Unlike the '399 patent, the presently claimed invention as a whole involves newly designed steps in which additional components are admixed with microparticles, e.g., as recited in steps (c) - (f) of the presently claimed invention, to arrive at Applicants' rapidly dispersible solid dosage form having the new and unobvious properties achieved according to the present invention.

However, without the teachings of Applicants' own invention, there is no disclosure or suggestion provided in the '399 patent that allows one skilled in the art to know to include the additional steps of admixing at least two matrix forming bulking/releasing agents with drug (e.g., cyclosporin)-containing microparticles, or during the formation of such microparticles, and drying the admixture to produce a rapidly dispersible solid drug dosage form in which drug-containing microparticles are dispersed and embedded in a solid support matrix having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the invention of Applicants.

The '399 patent simply does not teach or contemplate Applicants' process of producing a rapidly dispersible solid matrix form of a drug. Specific and nonobvious steps and components of Applicants' claimed process that are not supported by the disclosure and teaching of the '399 patent cannot *a priori* be determined to be included in the patent's process despite the use of comprising language in the claims. Accordingly, the '399 patent does not make obvious the presently amended claims. Withdrawal of this rejection is respectfully requested.

U.S. Patent No. 6,465,016

Claims 50-52, 54-75, 77-95, 97-104 and 107-131 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent No. 6,465,016 ("the '016 patent"). The Examiner states that the conflicting claims are not identical, but are allegedly not patentably distinct from each other

because the claims in the '016 patent, which are drawn to "a process of preparing microparticles of water insoluble drug, cyclosporine by mixing the drug, a phospholipid and another surfactant and applying energy to reduce particle sizes", recite comprising language and that "applicant's intent to include bulking material such as mannitol in the comprising language is clear from the examples" in the cited patent. The Examiner opines that the "instant steps of adding the bulking materials" are deemed to be included in the patented method claims and that "water insoluble drug includes cyclosporine" in the '016 patent claims.

Applicants disagree with this rejection and submit that although the claims of the '016 patent contain comprising language, there is no teaching or disclosure in the '016 patent that would lead one having skill in the art to arrive at Applicants' presently claimed process with a reasonable expectation of success.

Unlike the presently claimed invention, the '016 patent contains no teaching or disclosure of further steps other than those involved with making solid cyclic oligopeptide cyclosporin microparticles. The '016 patent contains no teaching or suggestion of admixing the disclosed microparticles with at least two matrix forming bulking/releasing agents or including at least two rapidly dispersible matrix-forming bulking/releasing agents during the process of preparing the microparticles, and drying the admixture so as to form a solid support matrix wherein drug particles are dispersed and embedded throughout and also wherein this support matrix dissolves or disperses in a rapid disintegration time when the solid matrix contacts an aqueous environment.

To assume that the comprising language of the claims of the '016 patent encompasses the particular steps recited in Applicants' presently claimed invention is also without basis, since the disclosure of the '016 patent does not teach the additional steps of admixing at least two matrix-forming bulking/releasing agents, or a combination of matrix-forming bulking agent and matrix-forming releasing agent to the microparticles described in the patent, and drying the admixture so as to produce a solid matrix having microparticles embedded and dispersed therein, wherein the solid matrix is rapidly dispersible in aqueous medium according to the additional steps of the presently claimed invention.

The combination of steps and elements of the presently claimed invention, including at least two matrix-forming bulking/releasing agents and combinations thereof, contributes to the newly described properties of high dispersibility imparted to the solid dosage drug form that is produced by Applicants' presently claimed process. The totality of the steps and elements that constitute the process of the presently claimed invention are not at all found in the disclosure of the '016 patent. The '016 patent claims a process of stabilizing cyclic oligopeptide cyclosporin microparticles. The patent does not teach Applicants' presently claimed method of preparing a rapidly dispersible solid dosage form containing drug microparticles.

In fact, the presently claimed process, while including the use of microparticles such as those described in the '016 patent, may be considered to further and extend the teaching of the '016 patent in a novel and unobvious way. Unlike the '016 patent, the presently claimed invention as a whole involves newly designed steps in which additional components are admixed with microparticles, e.g., as recited in steps (c) - (f) of the presently claimed invention, to arrive at Applicants' rapidly dispersible solid dosage form having the new and unobvious properties achieved according to the present invention.

However, without the teachings of Applicants' own invention, there is no disclosure or suggestion provided in the '016 patent that allows one skilled in the art to know to include additional steps of admixing at least two matrix forming bulking/releasing agents with drug (e.g., solid cyclic oligopeptide cyclosporin)-containing microparticles, or during the formation of such microparticles, and drying the admixture to produce a rapidly dispersible solid dosage form of the drug in which drug microparticles are dispersed and embedded in a solid support matrix having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the invention of Applicants.

The '016 patent simply does not teach or contemplate Applicants' process of producing a rapidly dispersible solid matrix form of a drug. Specific and nonobvious steps and components of Applicants' claimed process that are not supported by the disclosure and teaching of the '016 patent cannot *a priori* be determined to be included in the patent's process despite the use of comprising language in the claims. Accordingly, the '016 patent does not make obvious the presently amended claims. Withdrawal of this rejection is respectfully requested.

Co-pending patent application U.S. Serial No. 10/443,772

Claims 50-52, 54-75, 77-95, 97-104 and 107-131 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-44 of co-pending application U.S. Serial No. 10/443,772 ("the '772 application"). The Examiner states that the subject matter claimed in the instant application is fully disclosed in the co-pending '772 application, which is claiming common subject matter. According to the Examiner, the claims directed to "water insoluble drug" are deemed to include fenofibrate in the claims of the co-pending '772 application.

Applicants submit that this rejection has been repeated from the Office Action mailed March 30, 2005. In response to the rejection as first made in the prior Office Action, Applicants submitted an executed terminal disclaimer, accompanying documentation and fee. (*See*, Applicants' Amendment and response dated July 22, 2005). It is requested that the receipt and acceptability of these documents be acknowledged by the Patent Office. Accordingly, withdrawal of this rejection is requested.

Co-pending patent application U.S. Serial No. 10/260,788

Claims 50-52, 54-75, 77-95, 97-104 and 107-131 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 4-25, 45-47, 52, 53, 55, 56, 65 and 101-119 of co-pending application U.S. Serial No. 10/260,788 ("the '788 application"). The Examiner states that the conflicting claims are not identical, but they are allegedly not patentably distinct from each other because "the claims in the co-pending application are drawn to the same process of preparation and the products resulting from said process and the process is directed to water insoluble drugs." The Examiner further opines that the comprising language of the claims of the '788 application provides for the inclusion of a step of adding bulking materials such as mannitol, as claim 115 in the '788 application recites mannitol.

Applicants disagree with this provisional rejection and submit that although the claims of the '788 application contain comprising language, there is no teaching or disclosure in the '788 application that would lead one having skill in the art to arrive at Applicants' presently claimed

process with a reasonable expectation of success. Unlike the presently claimed invention, the '788 application contains no teaching or disclosure of further steps other than making the microparticles. The '788 application contains no teaching or suggestion of admixing the disclosed microparticles with at least two matrix forming bulking/releasing agents or including at least two rapidly dispersible matrix-forming bulking/releasing agents during the process of preparing the microparticles, and drying the admixture so as to form a solid support matrix wherein drug particles are dispersed and embedded throughout and also wherein this support matrix dissolves or disperses in a rapid disintegration time when the solid matrix contacts an aqueous environment.

The mere disclosure of mannitol in the Examples of the specification of the '788 application, and the recitation of mannitol as a stabilizing agent in the dependent claims of the '788 application, does not make obvious Applicants' inventive process, considered in its entirety. The cited application does not disclose a solid drug dosage form that is produced in accordance with Applicants' presently claimed process.

The steps and elements comprising the process of the presently claimed invention are nowhere found in the disclosure and claims of the '788 application, which are directed to a process for preparing solid microparticles of a water-insoluble of poorly water soluble compound in an aqueous medium. The '788 application contains no recognition of Applicants' presently claimed process.

The Examiner opines that because dependent claim 115 in the '788 application recites mannitol, it would therefore be obvious to include a step of adding mannitol to the process of the '788 application. Even if adding mannitol were to be included as a step in the claims of the '788 application, this does not make obvious the presently claimed invention. In distinction to the teachings of the '788 application, the presently claimed invention requires that at least two rapidly dispersible matrix-forming bulking/releasing agents, or a combination of a matrix-forming bulking agent and a matrix-forming releasing agent be added in the process to result in the formation of a solid support for drug-containing microparticles, thus yielding a dosage form containing drug microparticles that rapidly disperses upon contact with an aqueous environment. This teaching is not found or contemplated in the '788 application.

The '788 application simply does not teach or contemplate a rapidly dispersible form of a drug. There is also no teaching or suggestion provided in the '788 application that allows one skilled in the art to know to combine at least two bulking/releasing agents with an aqueous suspension of drug and surfactant/phospholipid in the amounts specified so that the steps and elements therein function to produce a solid dosage form of the drug having the disclosed properties of dispersibility. This nonobvious teaching is provided only by the Applicants according to the presently claimed invention. Accordingly, the '788 application does not disclose, exemplify or contain all of the steps and elements of the presently claimed invention and thus does not make obvious the presently amended claims. Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicants respectfully submit that the present application is now in condition for allowance or in better form for appeal. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this Amendment, or during the pendancy of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**; Reference No. **28069-546**; Customer No. **35437**.

Should any further extension of time be required for the timely consideration of this Amendment and response, the Commissioner is hereby authorized to grant any such further extension of time as may be necessary, and to charge any additional fee(s) owed by Applicants for such extension of time, to the above-mentioned Deposit Account, Reference and Customer Numbers.

If the Examiner believes that further discussion of the application would be helpful, he is respectfully requested to telephone Applicants' undersigned representative at (212) 692-6742 and is assured of full cooperation in an effort to advance the prosecution of the instant application and claims to allowance.

Respectfully submitted,
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.

Date: March 10, 2006

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